COMPUTATIONAL MODELING OF [Ca^{2+}] OSCILLATIONS IN ASTROCYTES USING THE MATHEMATICAL THEORY OF KNOTS

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Calcium oscillations have numerous functions in a wide variety of cells and are integral to the regulation of many biological processes. Their known functions range from the regulation of heart beats, circadian rhythms, and hormone secretion to roles in the fertilization and wound healing processes. They are also present in other cells, such as astrocytes (the most abundant cell type in the central nervous system), in which their function remains unknown.

This study utilizes the astrocytic calcium system that we have previously explored. The model consists of a system of three differential equations, which describe [Ca^{2+}] oscillations in the cytosol, mitochondria, and endoplasmic reticulum of astrocytes. Numerical integration, using the Gear algorithm, is used to produce concentration vs. time data that can be compared to experimental data. $[Ca2+]_{cyt}$ vs. $[Ca2+]_{ER}$ vs. $[Ca2+]_{mit}$ can be plotted to produce 3-dimensional phase portraits. Comparison of these plots reveals the large change from simple periodic to chaotic behavior when only a single parameter (most notably, the fractional external stimulation) is changed; this is consistent with experiment. It is known that dynamical systems in a chaotic regime can tie themselves into knots in 3-D space. We are probing for knots in chaotic phase planes and using the principles of knot theory to tie the governing mathematics to the biological behavior.

The mathematics of knot theory may prove to be very important when applied to dynamic biological systems. From a biochemical point of view, the concept of knot invariance under continuous transformations implies that a periodic (unknotted) state cannot move to a chaotic (knotted) state by way of a continuous transformation; we want to show that certain types of behavior are invariant under this set of topological principles. We will demonstrate that periodic behavior of any period is topologically equivalent to any other periodic behavior, but is not topologically equivalent to certain types of chaotic behavior. We plan to characterize aspects of this biological system according to the mathematical operations and transformations that are permitted by the rules of know theory; find biological parameters for which the system is invariant to a change in value; and gain further insight into how a system moves from a chaotic to a periodic regime when a continuous transformation of this type is not possible.